CLAIMS

WHAT IS CLAIMED IS:

1. An *in vitro* method for measuring the genomic replication of a virus that is dependent for replication upon RNA-dependent RNA polymerase (an RDRP virus) comprising the steps of:

a) culturing virally-compatible eukaryotic cells which have been transfected with the cDNA of the genomic sequence of said RDRP virus;

b) transfecting said cultured cells with a construct comprising the cDNA, in antisense orientation, of a reporter gene sequence wherein said reporter gene cDNA sequence is operably linked on its 5′ end with the cDNA of the untranslated region (UTR), in antisense orientation, of the native 3′ end of said RDRP virus and is operably linked on its 3′ end with the cDNA of the UTR, in antisense orientation, of the native 5′ end of said RDRP virus;

c) culturing said cells for a sufficient period of time under conditions which are permissive for replication of said RDRP virus; and

d) analyzing the cells for the presence of the protein encoded by the reporter gene sequence,

whereby detection of said protein provides a means to measure the genomic replication of said RDRP virus.

2. The method of Claim 1, wherein the RDRP virus is a member of the *Flaviviridae* family.

3. The method of Claim 2, wherein the RDRP virus is HCV.

4. The method of Claim 1, wherein the virally-compatible eukaryotic cell is human.

5. The method of Claim 4, wherein the virally-compatible eukaryotic cell is a human liver or kidney cell.

6. The method of Claim 3, wherein the virally-compatible eukaryotic cells of step (a) are from the human cell line 293 FL#9.

7. The method of Claim 1 wherein at step (b), transfection of cultured cells is performed using the method selected from: electroporation, liposomal transfer, $CaPO_4$ shock, and DEAE-dextran shock.

8. The method of Claim 1, wherein at step (b), the construct further comprises the cDNA, in the sense orientation, of a delta ribozyme operably linked to the 3' end of the 5' UTR sequence.

9. The method of Claim 1, wherein the reporter gene is selected from: luciferase, secreted alkaline phosphatase, beta-galactosidase, Hepatitis B virus surface antigen, herpes simplex virus thymidine kinase, genticin-resistance, zeocin-resistance, hygromycin-resistance, and puromycin-resistance.

10. The method of Claim 9, wherein the reporter gene is luciferase.

11. The method of Claim 3, wherein at step (b) the construct further comprises the cDNA, in sense orientation,

of the hepatitis delta ribozyme operably linked to the end of the 5' UTR sequence.

12. The method of claim 3 wherein the construct at step (b) comprises SEQ ID NO: 18.

13. The method of claim 6 wherein the construct at step (b) comprises SEQ ID NO: 18.

14. A construct comprising the cDNA in antisense orientation of a reporter gene sequence wherein said reporter gene cDNA sequence is operably linked on its 5' end with the cDNA of the untranslated region (UTR), in antisense orientation, of the native 3' end of an RDRP virus and is operably linked on its 3' end with the cDNA of the UTR, in antisense orientation, of the native 5' end of the RDRP virus.

15. The construct of Claim 14, wherein the RDRP virus is HCV.

16. The construct of Claim 14, wherein the construct further comprises the cDNA, in sense orientation, of the hepatitis delta ribozyme operably linked to the 3' end of the 5' UTR sequence.

17. The construct of Claim 16, wherein the RDRP virus is HCV, and the reporter gene is selected from: luciferase, secreted alkaline phosphatase, beta-galactosidase, hepatitis B virus surface antigen, herpes simplex virus thymidine kinase, genticin-resistance, zeocin-resistance, hygromycin-resistance, and puromycin-resistance.

18. A construct comprising SEQ ID NO:17.

19. A cell containing the construct of Claim 14.

20. A cell containing the construct of Claim 16.

21. A 293B4α cell.

22. An *in vitro* method for identifying compounds or conditions which inhibit the genomic replication of a virus that is dependent for replication on RNA-dependent RNA polymerase (an RDRP virus) comprising the steps of:

a) culturing virally-compatible eukaryotic cells which have been transfected with the cDNA of all or a portion of the genomic sequence of said RDRP virus;

b) transfecting said cultured cells with a construct comprising the cDNA, in antisense orientation, of a reporter gene sequence wherein said reporter gene cDNA sequence is operably linked on its 5′ end with the cDNA of the untranslated region (UTR), in antisense orientation, from the native 3′ end of said RDRP virus and is operably linked on its 3′ end with the UTR, in antisense orientation, from the native 5′ end of said RDRP virus;

c) exposing said cultured cells to a compound or condition suspected of being capable of inhibiting the genomic replication of said RDRP virus;

d) culturing said cells for a sufficient period of time under conditions which are permissive for genomic replication of said RDRP virus; and

e) analyzing the cells for the presence of the

protein encoded by the reporter gene sequence, whereby a decrease in the level of said protein encoded by the reporter gene sequence indicates that said compound or condition is capable of inhibiting the genomic replication of said RDRP virus.

23. The method of Claim 22, wherein the RDRP virus is a member of the *Flaviviridae* family.

24. The method of Claim 23, wherein the RDRP virus is HCV.

25. The method of Claim 22, wherein the virally-compatible eukaryotic cell is human.

26. The method of Claim 25, wherein the virally compatible eukaryotic cell is a liver or kidney cell.

27. The method of Claim 22, wherein the virally-compatible eukaryotic cells of step (a) are from the human cell line 293 FL#9.

28. The method of Claim 22 wherein at step (b), transfection of cultured cells is performed using the method selected from: electroporation, liposomal transfer, $CaPO_4$ shock, and DEAE-dextran shock.

29. The method of Claim 22, wherein at step (b), the construct further comprises the cDNA, in the sense orientation, of a delta ribozyme sequence operably linked to the 3′ end of the 5′ UTR sequence.

30. The method of Claim 22, wherein the reporter gene

is selected from: luciferase, secreted alkaline phosphatase, beta-galactosidase, hepatitis B virus surface antigen, herpes simplex virus thymidine kinase, genticin-resistance, zeocin-resistance, hygromycin-resistance, and puromycin-resistance.

31. The method of Claim 30, wherein the reporter gene is luciferase.

32. The method of Claim 24, wherein at step (b) the construct further comprises the cDNA, in sense orientation, of the hepatitis delta ribozyme operably linked to the end of the 5' UTR sequence.

33. The method of Claim 22, wherein said compound or condition is selected from the group consisting of: small molecular weight synthetic chemicals, organic compounds that are derived from living or once living organisms, synthetic chemical compounds based on organic compounds derived from living or once living organisms, sound, light and temperature.

34. The method of Claim 33 wherein said compound is a small molecular weight synthetic chemical.

35. The method of Claim 32, wherein at step (a) said virally compatible cells have been transfected with the cDNA of all of the genomic sequence of HCV.

36. The method of Claim 24, wherein at a step (a) said portion of the genomic sequence of said RDRP virus consists essentially of the genomic sequences encoding from the NS2 to the NS5b region.

37. The method of Claim 24, wherein at a step (a) said portion of the genomic sequence of said RDRP virus consists essentially of the genomic sequence encoding the NS5b portion.

38. The method of Claim 35 wherein the cultured cells at step (e) are 293B4α cells.

39. The method of claim 24 wherein the construct of step (b) comprises SEQ ID NO: 18.

40. A method of selectively affecting a cell infected with a virus that is dependent for genomic replication upon RNA-dependent RNA polymerase (an RDRP virus) comprising the steps of:

a) transfecting said infected cell with a construct comprising the cDNA, in antisense orientation, of a gene sequence which encodes a protein that is capable of affecting said cell, wherein said cDNA sequence is operably linked on its 5′ end with the cDNA of the untranslated region (UTR), in antisense orientation, of the native 3′ end of said RDRP virus and is operably linked on its 3′ end with the cDNA of the UTR, in antisense orientation, of the native 5′ end of said RDRP virus; and

b) allowing a sufficient period of time for genomic replication of said RDRP virus,

whereby upon genomic replication of said RDRP virus, RNA-dependent RNA polymerase produced by said replicating RDRP virus will cause expression of the construct of step (a), whereby the cell is affected.

41. The method of Claim 40, wherein the RDRP virus is HCV.

42. The method of Claim 40, wherein at step (a) the construct further comprises the cDNA of a delta ribozyme sequence, in sense orientation, operably linked to said 3' end of the cDNA of the UTR, in antisense orientation of the native 5' end of said RDRP virus.